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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,158	09/25/2006	Samuel J. Danishefsky	2003080-0201 (SK-1071-US1	3195

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EXAMINER	
HAVLIN, ROBERT H	
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1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,158	DANISHEFSKY ET AL.	
	Examiner	Art Unit	
	ROBERT HAVLIN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-37,48-64 and 71-78* is/are pending in the application.

4a) Of the above claim(s) *6,14-19,21,22,25-33,36,37,48,56-64,74 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-13,23,24,34,35,49-55,71-73 and 76-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

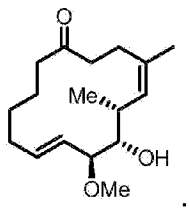
Status of the claims: Claims 1-19, 21-37, 48-64, and 71-78 are currently pending.

Priority: This application is a 371 of PCT/US04/09571 (03/26/2004).

IDS: The IDS dated 1/13/10 was considered.

Election/Restrictions

1. Applicant previously elected group III (claims 1-37, 48-55, and 71-78) and the following species (stated to read on claims 1-5, 7-13, 23-24, 34-35, 49-64, 71-73, and 76-78):



As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and claims not reading on the elected species are held withdrawn. Accordingly, claims 6, 14-19, 21-22, 25-33, 36-37, 48, 56-64, and 74-75 are hereby withdrawn.

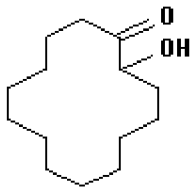
Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP 803.02.

RESPONSE TO APPLICANT REMARKS

Claim Rejections - 35 USC § 102

2. Claims 1, 2, and 49 were rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2002), 41B(2), 423-426).

Singh et al. teaches the following compound:



Applicant has amended the claims to delete alternatives of R6 that read on the prior art. Therefore, this rejection is **withdrawn**.

Claim Rejections - 35 USC § 112

3. Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73, and 76-78 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds identified as having the asserted utility with experimental data, does not reasonably provide enablement for the asserted utility of the entirety of the claim scope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has narrowed the scope of the claims in a manner that is consistent with the enabling disclosure. This rejection is **withdrawn**.

Double Patenting

4. Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73, and 76-78 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42, 45-47 of copending Application No. 10/551152 (*previously mistakenly referred to as 10/555152*).

Applicant has requested this rejection be held in abeyance until the claims are in condition for allowance. Accordingly, this rejection is **maintained**.

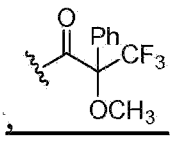
NEW REJECTIONS

Claim Rejections - 35 USC § 112

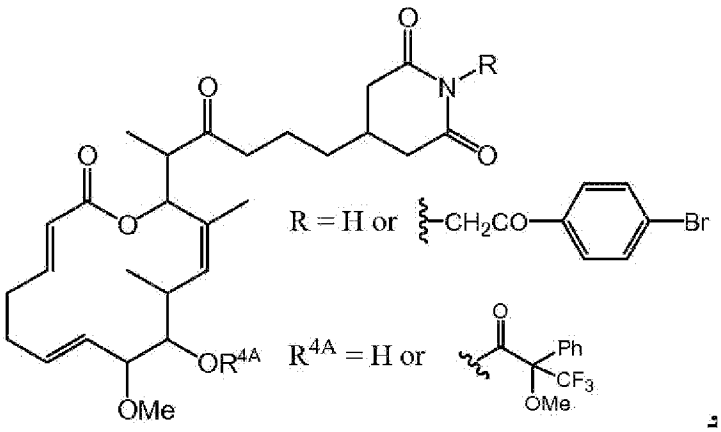
5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1, 2, 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

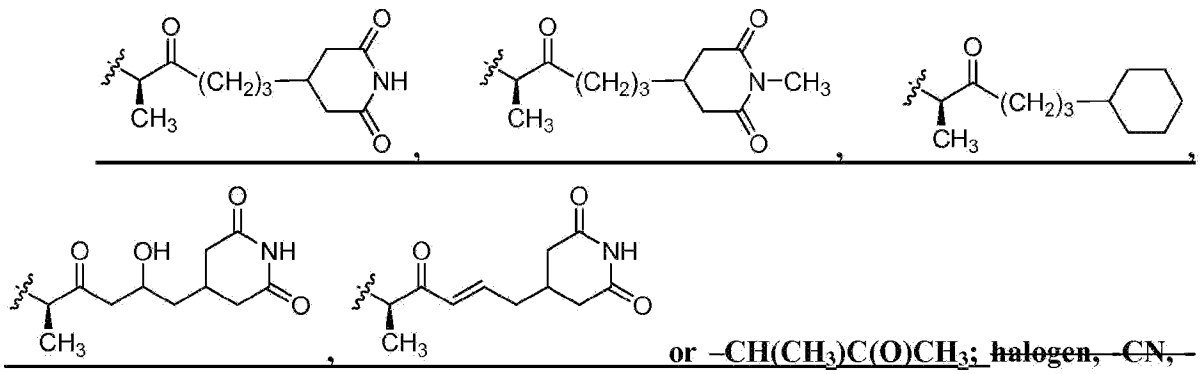
The claims amendments of 7/8/09 contained amendments that are not supported by the original claims or the specification. In particular, the variable R4 includes the new alternative of 

. It appears that the applicant intended to import this alternative from a proviso definition of R4a as follows:



however, this is not a sufficient description such that one of skill in the art would recognize applicant as being in possession of the new alternative of R4.

Similarly, the variable Q lists the following new alternatives:



without specific support in the claims or specification, nor are there sufficient representative species to support this new subgenus.

7. Claims 1, 25, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for “pharmaceutically acceptable derivatives” thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This phrase is defined in the specification as:

> **[0027]** The phrase, "pharmaceutically acceptable derivative", as used herein, denotes any pharmaceutically acceptable salt, ester, or salt of such ester, of such compound, or any other adduct or derivative which, upon administration to a patient, is capable of providing (directly or indirectly) a compound as otherwise described herein, or a metabolite or residue thereof. Pharmaceutically acceptable derivatives thus include among others pro-drugs. A pro-drug is a derivative of a compound, usually with significantly reduced pharmacological activity, which contains an additional moiety, which is susceptible to removal *in vivo* yielding the parent molecule as the pharmacologically active species. An example of a pro-drug is an ester, which is cleaved *in vivo* to yield a compound of interest. Pro-drugs of a variety of compounds, and materials and methods for derivatizing the parent compounds to create the pro-drugs, are known and may be adapted to the present invention. Certain exemplary pharmaceutical compositions and pharmaceutically acceptable derivatives will be discussed in more detail herein below.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of Invention. The nature of the invention involves pharmaceutical compounds including forms unknown ("any other adduct or derivative" or "pro-drug").

Scope of the Invention. The scope of the invention is for a genus of compounds of formula I which substantially varies in structure and has in excess of millions of species before considering any derivative thereof.

State of the Art and Level of Skill in the Art. The formation of prodrugs or unknown derivatives is highly unpredictable due to the potential physical or chemical interactions of the prodrug moiety with the base drug. Bundgaard (Design and application of prodrugs, In A Textbook of Drug Design and Development, (1991), p 113-191) teaches that there are numerous unpredictable factors that can affect the particular pharmacokinetics including the detailed structure of the molecule as it interacts with the prodrug moiety. Furthermore, providing a compound "directly or indirectly" would also be highly unpredictable for the same reasons as described by Bundgaard.

Number of Working Examples and Guidance Provided by Applicant. The applicant provides no working examples or guidance regarding prodrugs or derivatives.

Unpredictability of the Art and Amount of Experimentation. The formation of derivatives or prodrugs is highly unpredictable and one of ordinary skill in the art could not predict whether a particular derivative would be useful. To determine this requires trial and error experimentation that would be an undue burden. This burden also results from a huge amount of experimentation required in order to synthesize and screen the millions of compounds within the claimed scope for any possible prodrug or derivative that would be useful. In addition, one of skill in the art could not predict whether any particular prodrug form would function without synthesizing, screening, and testing each form because of the complex physical interactions between the prodrug moiety, the underlying pharmaceutical and the environment. The burden is particularly high in this context due to the large number of underlying compounds within the claim scope that would need to be synthesized and tested.

Considering the above factors, the claims are not enabled for derivatives of the compounds claimed. The examiner recommends replacing "derivative" with "salt" or something similar.

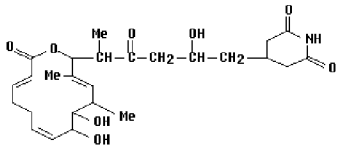
Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-5, 9, 10, 13, 23-24, and 49-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Isogai et al. (STN Abstract of JP 07138257 A).

The prior art reference teaches the following compound as a bone absorption inhibitor:

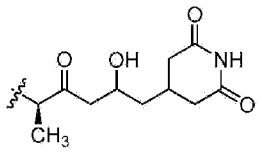


which reads on the instant claims when:

R1, R2, R3, Ra, Rb, Rc are H

R4 is –OH

R5, R6 are –Me

Q is 

X1 is –O-

C(Y1)(Y2) form –C(O)-.

Conclusion

The claims are not in condition for allowance.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner, Art Unit 1626